- binds to the mutated MBP or forms a complex including the mutated MBP, and which preferentially inhibits proliferation of T cells expressing the mutated MBP relative to T cells expressing wild-type MBP.
- 4. (Amended) The method of claim 1, wherein the macrolide binds to or forms a complex with the mutated MBP with a dissociation constant, Kd, at least one order of magnitude less than its Kd for binding to or forming a complex with wild-type MBP.
- 5. (Amended) The method of claim 4, wherein the macrolide binds to or forms a complex with the mutated MBP with a dissociation constant, Kd, at least three orders of magnitude less than its Kd for binding to or forming a complex with wild-type MBP.
- 6. (Amended) The method of claim 1, wherein the MBP gene was introduced into the cell ex vivo by DNA transfection.
- 7. (Amended) The method of claim 1, wherein the MBP gene was introduced into the cell *ex vivo* by virus-mediated transduction.
- 8. (Amended) The method of claim 1, wherein the MBP gene was introduced into the cell *ex vivo* by homologous recombination.
- 9. (Amended) The method of claim 1, wherein the macrolide is an analog of rapamycin, FK506 or cyclosporin.
- 10. (Amended) The method of claim 1, wherein the MBP gene encodes a FRAP protein, and the macrolide is an analog of rapamycin.
- 11. (Amended) The method of claim 1, wherein the MBP gene encodes an FK506 binding protein, and the macrolide is an analog of FK506 or rapamycin.
- 12. (Amended) The method of claim 1, wherein the MBP gene encodes a calcineurin protein, and the macrolide is an analog of FK506 or cyclosporin.
- 13. (Amended) The method of claim 1, wherein the MBP gene encodes a cyclophilin protein, and the macrolide is an analog of cyclosporin.
- 14. (Amended) The method of claim 1, wherein the cell is a mammalian cell.
- 15. (Amended) The method of claim 1, wherein the cell is a human cell.

- 16. (Amended) A method for preferentially inhibiting genetically engineered T cells in an animal, wherein the genetically engineered T cells include a recombinant gene encoding a mutated macrolide binding protein (MBP) selected from an FK506-binding protein (FKBP), cyclophilin, calcineurin, and FKBP:rapamycin associated protein (FRAP), which method comprises:
 - (i) introducing into the animal, genetically engineered T cells which include a recombinant gene encoding the mutated MBP, and
 - (ii) administering to the animal a macrolide which binds to the mutated MBP or forms a complex including the mutated MBP, and which preferentially inhibits proliferation of T cells expressing the mutated MBP relative to T cells expressing wild-type MBP.
- 18. (Amended) The method of claim 16, wherein the macrolide binds to or forms a complex with the mutated MBP with a dissociation constant, Kd, at least one order of magnitude less than its Kd for binding to or forming a complex with wild-type MBP.
- 19. (Amended) The method of claim 16, wherein the macrolide binds to or forms a complex with the mutated MBP with a dissociation constant, Kd, at least three orders of magnitude less than its Kd for binding to or forming a complex with wild-type MBP.
- 20. (Reiterated) The method of claim 16, wherein the MBP gene was introduced into the cell *ex vivo* by DNA transfection.
- 21. (Reiterated) The method of claim 16, wherein the MBP gene was introduced into the cell *ex vivo* by virus-mediated transduction.
- 22. (Reiterated) The method of claim 16, wherein the MBP gene was introduced into the cell *ex vivo* by homologous recombination.
- 23. (Reiterated) The method of claim 16, wherein the macrolide is an analog of rapamycin, FK506 or cyclosporin.
- 24. (Reiterated) The method of claim 16, wherein the animal is a mammal.
- 25. (Reiterated) The method of claim 24, wherein the animal is a human.

- 26. (Amended) The method of claim 16, wherein the introduced T cells are autologous, allogeneic or xenogeneic to the animal.
- 29. (Reiterated) The method of claim 16, wherein the expression of the mutated MBP gene is transcriptionally regulated by a T-cell specific transcriptional regulatory sequence.
- 32. (Amended) An expression construct encoding a mutated macrolide binding protein (MBP) selected from an FK506-binding protein (FKBP), cyclophilin, calcineurin, and FKBP:rapamycin associated protein (FRAP), wherein the mutated MBP binds to or forms a complex with a macrolide which preferentially inhibits proliferation of T cells expressing the mutated MBP relative to T cells expressing wild-type MBP.
- 33. (Amended) A kit for preferentially inhibiting T cells, comprising
 - (i) an expression construct of claim 32 encoding a mutated MBP, and
 - (ii) a macrolide which binds to the mutated MBP or forms a complex including the mutated MBP, and which preferentially inhibits proliferation of T cells expressing the mutated MBP relative to T cells expressing wild-type MBP.
- 36. (Amended) An isolated population of cells comprising T cells which include a recombinant gene encoding a mutated macrolide binding protein (MBP) selected from an FK506-binding protein (FKBP), cyclophilin, calcineurin, and FKBP:rapamycin associated protein (FRAP), wherein the mutated MBP binds to or forms a complex with a macrolide, and treatment with the macrolide preferentially inhibits proliferation of T cells expressing the mutated MBP relative to T cells expressing wild-type MBP.
- 38. (Amended) A method for rendering T cells susceptible to preferential inhibition, which method comprises introducing into the T cells the expression construct of claim 32.
- 39. (Amended) The method for providing an animal with preferentially inhibitable T cells, comprising introducing into the animal preferentially inhibitable T cells prepared by the method of claim 38.
- 44. (Reiterated) The expression construct of claim 32, which encodes a mutated FKBP or cyclophilin.

懂:

The claims presented above incorporate changes as indicated by the marked-up versions below.

- 1. (Amended) A method for <u>preferentially</u> inhibiting [activation of a] T cells[, wherein the T cell or a progenitor cell thereof was engineered *ex vivo* to express] which include a recombinant gene encoding a mutated macrolide binding protein (MBP) selected from an FK506-binding protein (FKBP), cyclophilin, calcineurin, and FKBP:rapamycin associated protein (FRAP), which method comprises contacting the cell with a macrolide which binds to the mutated MBP or forms a complex including the mutated MBP, and which preferentially [induces macrolide-dependent inhibition of activation of the T cell in a manner dependent on the expression of the mutated MBP] inhibits proliferation of T cells expressing the mutated MBP relative to T cells expressing wild-type MBP.
- 4. (Amended) The method of claim 1 [or 2], wherein the macrolide binds to or forms a complex with the mutated MBP with a dissociation constant, Kd, at least one order of magnitude less than its Kd for binding to or forming a complex with wild-type MBP.
- 5. (Amended) The method of claim 4, wherein the macrolide binds to or forms a complex with the mutated MBP with a dissociation constant, Kd, at least three orders of magnitude less than its Kd for binding to or forming a complex with wild-type MBP.
- 6. (Amended) The method of claim 1 [or 2], wherein the MBP gene was introduced into the cell *ex vivo* by DNA transfection.
- 7. (Amended) The method of claim 1 [or 2], wherein the MBP gene was introduced into the cell *ex vivo* by virus-mediated transduction.
- 8. (Amended) The method of claim 1 [or 2], wherein the MBP gene was introduced into the cell *ex vivo* by homologous recombination.
- 9. (Amended) The method of claim 1 [or 2], wherein the macrolide is an analog of rapamycin, FK506 or cyclosporin.
- 10. (Amended) The method of claim 1 [or 2], wherein the MBP gene encodes a FRAP protein, and the macrolide is an analog of rapamycin.
- 11. (Amended) The method of claim 1 [or 2], wherein the MBP gene encodes an FK506 binding protein, and the macrolide is an analog of FK506 or rapamycin.

- 12. (Amended) The method of claim 1 [or 2], wherein the MBP gene encodes a calcineurin protein, and the macrolide is an analog of FK506 or cyclosporin.
- 13. (Amended) The method of claim 1 [or 2], wherein the MBP gene encodes a cyclophilin protein, and the macrolide is an analog of cyclosporin.
- 14. (Amended) The method of claim 1 [or 2], wherein the cell is a mammalian cell.
- 15. (Amended) The method of claim 1 [or 2], wherein the cell is a human cell.
- 16. (Amended) A method for [selectively] <u>preferentially</u> inhibiting <u>genetically engineered</u> T cells [activation] in [a transplanted T cell comprising] <u>an animal, wherein the genetically engineered T cells include</u> a <u>recombinant gene encoding a mutated macrolide binding protein (MBP) selected from an FK506-binding protein (FKBP), cyclophilin, calcineurin, and FKBP:rapamycin associated protein (FRAP), which method comprises:</u>
 - (i) [transplanting,] introducing into [an] the animal, [a T cell or a progenitor cell thereof, which T cell or progenitor cell thereof which has been engineered ex vivo to express an MBP gene encoding a mutated macrolide binding protein (MBP), the mutated MBP having an altered macrolide-binding specificity relative to the wild-type form MBP,] genetically engineered T cells which include a recombinant gene encoding the mutated MBP, and
 - (ii) administering to the animal [an amount of] a macrolide [sufficient to inhibit activation of the transplanted T cell or progenitor cell thereof, which macrolide selectively induces macrolide-dependent inhibition of activation of the transplanted T cell, in a manner dependent on the expression of the mutated MBP, when compared to cells expressing a wild-type form of the MBP] which binds to the mutated MBP or forms a complex including the mutated MBP, and which preferentially inhibits proliferation of T cells expressing the mutated MBP relative to T cells expressing wild-type MBP.
- 18. (Amended) The method of claim 16, wherein the macrolide binds to or forms a complex with the mutated MBP with a dissociation constant, Kd, at least one order of magnitude less than its Kd for binding to or forming a complex with wild-type MBP.

- 19. (Amended) The method of claim 16, wherein the macrolide binds to or forms a complex with the mutated MBP with a dissociation constant, Kd, at least three orders of magnitude less than its Kd for binding to forming a complex with wild-type MBP.
- 26. (Amended) The method of claim 16, wherein the [transplanted] introduced T cells [is] are autologous, allogeneic or xenogeneic to the animal.
- 32. (Amended) An expression construct encoding a mutated [FRAP, FKBP, cyclophilin or calcineurin, wherein the mutated protein has an altered macrolide-binding specificity relative to its wild-type form and, in the presence of a macrolide to which it binds, induces macrolide-dependent inhibition of activation of a T cell expressing the mutated protein] macrolide binding protein (MBP) selected from an FK506-binding protein (FKBP), cyclophilin, calcineurin, and FKBP:rapamycin associated protein (FRAP), wherein the mutated MBP binds to or forms a complex with a macrolide which preferentially inhibits proliferation of T cells expressing the mutated MBP relative to T cells expressing wild-type MBP.
- 33. (Amended) A kit for [selectively] <u>preferentially</u> inhibiting [activation of a] T cells, comprising
 - (i) an expression construct of claim 32 encoding a mutated MBP, and
 - (ii) a macrolide which [selectively binds to the altered protein relative to the wild-type protein and selectively induces macrolide-dependent inhibition of activation of T cells expressing the mutated MBP relative to T cells expressing only the wild-type MBP] binds to the mutated MBP or forms a complex including the mutated MBP, and which preferentially inhibits proliferation of T cells expressing the mutated MBP relative to T cells expressing wild-type MBP.
- 36. (Amended) An isolated population of cells comprising [a] T cells [or progenitor cell thereof, which is transfected with an expression construct of claim 32] which include a recombinant gene encoding a mutated macrolide binding protein (MBP) selected from an FK506-binding protein (FKBP), cyclophilin, calcineurin, and FKBP:rapamycin associated protein (FRAP), wherein the mutated MBP binds to or forms a complex with a